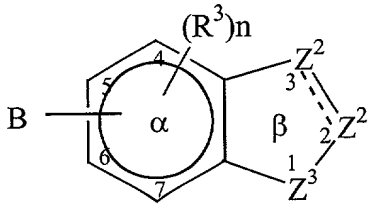
Abstract

The invention is directed to methods to inhibit p38-α kinase using compounds of the formula



(1)

and the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof, wherein

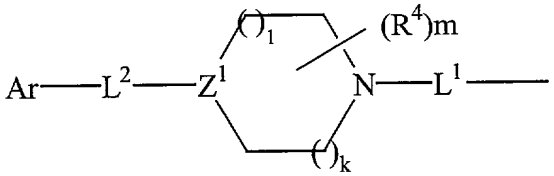
represents a single or double bond;

B is $-W_i-COX_jY$ wherein Y is COR^2 or an isostere thereof and R^2 is hydrogen or a noninterfering substituent, each of W and X is a spacer of 2-6Å, and each of i and j is independently 0 or 1;

each R^3 is independently a noninterfering substituent, where n is 0-3;

Z^3 is NR^7 or O; wherein R^7 is H or a noninterfering substituent;

one Z^2 is CA or CR^8A and the other is CR^1, CR^1_2, NR^6 or N wherein each R^1, R^6 and R^8 is independently hydrogen or noninterfering substituent; wherein A is:



such that Z^1 is CR^5 or N wherein R^5 is hydrogen or a noninterfering substituent;

each of l and k is an integer from 0-2 wherein the sum of l and k is 0-3;

Ar is an aryl group substituted with 0-5 noninterfering substituents, wherein two noninterfering substituents can form a fused ring;

each R^4 is independently a noninterfering substituent where m is 0-4;

each of L^1 and L^2 is a linker; and

the distance between the atom of Ar linked to L^2 and the center of the β ring is 4.5-24Å.